

REMARKS

In response to the Non-Final Office Action dated November 15, 2010, Applicants provide the following remarks that are made without prejudice to the prosecution of any subject matter in a related divisional, continuation or continuation-in-part application. Claims 1-30 are pending. Claims 4, 13, 15 and 16 have been amended. Claims 1-3, 5-12, 14 and 17-30 have been withdrawn from consideration.

Each of claims 4, 13, 15 and 16 have been amended for clarity. Claim 4 has been amended to recite values for Y, W1, W2, W4, Z1, Z2, Z3, Z4, Z5, Z6 and n. In addition, each of claims 4, 13, 15 and 16 have been amended to recite an embodiment wherein the metal comprises a surface which enables diffuse reflection of a laser beam.

The above amendments are fully supported by the specification as filed. For example, an embodiment wherein the metal comprises a surface which enables a diffuse reflection of a laser beam is described on page 30, line 30. Support for the values of the variables recited in claim 4 can be found at page 76, line 29 to page 77, line 7. Accordingly, no new matter has been added by way of this amendment.

Rejection Under 35 U.S.C. § 112

Claim 4 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner believes this claim is indefinite because the variables recited in the claim are not defined. As noted above, claim 4 has been amended to recite values for Y, W1, W2, W4, Z1, Z2, Z3, Z4, Z5, Z6 and n. Accordingly, Applicants submit that claim 4 is sufficiently definite and request that this ground of rejection be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 4 and 13 stand rejected under 35 U.S.C § 103 as being unpatentable over U.S. Patent Application Pub. No. 2005/0074551 ("Huang") in view of PCT Pub. No. WO 98/59362 ("Hutchens"), and claims 15 and 16 stand rejected under 35 U.S.C § 103 as being unpatentable over Hutchens in view of U.S. Patent No. 4,511,658 ("Lambert"). In short, the

Examiner is of the opinion that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of the above disclosures to arrive at the claimed invention. Applicants respectfully disagree.

Claims 4, 13, 15 and 16 each recite a metal-organic residue complex, wherein the metal comprises a surface which enables diffuse reflection of a laser beam. Claims 4, 15 and 16 are directed to methods for mass spectrometric analysis comprising ionizing the metal-organic residue complex bound to a sugar chain or sugar chain-containing substance. Claim 13 is directed to a method for trapping a sugar chain or a sugar chain-containing substance. Such trapping methods are useful, for example, for mass spectrometric analysis of the sugar chain or sugar chain-containing substance.

The recited methods may be used for accurate real-time monitoring of enzymatic reactions related to sugar chains. In this regard, Applicants have unexpectedly discovered that highly sensitive mass spectrometric analyses of sugar chains or sugar chain-containing substances are possible when the sugar chain or sugar chain containing substance is attached, via a sulfur-containing linker, to a metal comprising a surface which enables diffuse reflection of a laser beam. Such analyses can be made even in the presence of high concentrations of buffers or salts, and in certain embodiments, the recited methods do not require the use of a matrix component, thus allowing sensitive detection of low molecular weight regions (see *e.g.*, specification at page 30, line 26 to page 31, line 8 and Example 18). These aspects of the claimed subject matter are not taught, much less suggested, by the cited art.

Huang is directed to the fabrication of nanodevices comprising biological molecules (*e.g.*, proteins and nucleic acids) attached to nanoparticles (Huang at paragraph [0045]). With respect to analysis, Huang discloses that proteins attached to nanoparticles can be analyzed by gel electrophoresis and ion exchange chromatography (Huang Examples 6 and 7). However, in no instance does Huang teach or suggest a sugar chain or sugar chain-containing substance attached to a metal comprising a surface which enables a diffuse reflection of a laser beam or that the same can be analyzed by mass spectrometry at such increased sensitivity. Clearly such a teaching cannot lead one of skill in the art to the claimed subject matter.

Hutchens does not cure the deficiencies of Huang. Hutchens discloses retentate chromatography methods comprising chip arrays. Hutchens notes that analytes (*e.g.*, proteins) can be separated based on their ability to adsorb to an adsorbent (Hutchens at page 4, lines 6-8), and these adsorbants can be attached to a substrate (*e.g.*, a metal) in an array of pre-determined, addressable locations (Hutchens at page 4, lines 31-32 and page 7, lines 17-20). Substrates disclosed by Hutchens include strips, plates and substrates removably insertable into a detector (Hutchens at page 27, lines 18-23 and page 28, lines 29-30). This is in stark contrast to the recited methods wherein the sugar chain or sugar chain-containing substance is attached to a metal comprising a surface which enables diffuse reflection of a laser beam (*e.g.*, fine metal particles, see specification at page 37, line 27 to page 38, line 2), and the mass spectrometric analysis is performed on a solution comprising the metal, rather than a fixed array (specification at page 31, lines 3-4).

Lambert is directed to a colorimetric analysis for formaldehyde comprising the use of a 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole (AHMT) ketone amination (Lambert at column 1, lines 46-66). Lambert does not provide any teaching or suggestion to use AHMT, or any other organic residue, in a mass spectrometric analysis comprising ionization of a sugar chain or sugar chain-containing substance attached to a metal.

In summary, the cited references, either alone or in combination, clearly do not teach or suggest the recited methods or the above noted increased sensitivity of the same. Huang is directed to electrophoresis and ion chromatography methods and provides no motivation to modify the array-based method of Hutchens to arrive at the recited solution-based mass spectrometry methods comprising enhanced sensitivity. Finally, Lambert simply notes that formaldehyde may be detected based on a color change upon reaction with AHMT, and both Hutchens and Lambert are devoid of any motivation to combine such formaldehyde detection methods with Hutchens' disclosure to obtain the claimed subject matter. Accordingly, Applicants submit that the pending claims are patentable over the cited references (*i.e.*, nonobvious) and request that this ground of rejection be withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable.
Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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